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EXAMINER	
WHITEMAN, BRIAN A	
ART UNIT	**PAPER NUMBER**
1635	15

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/658,537	PATON ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 July 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-119* is/are pending in the application.

4a) Of the above claim(s) *10-14, 16-24,26-35,38-40,42,44,71,86-87,92-93,95-96,108,109,111-116* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,15,25,36,37,41,43,45-70,72-85,88-91,94,97-107,110 and 117-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☒ The proposed drawing correction filed on *07 November 2002* is: a)☒ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

DETAILED ACTION

Final Rejection

Claims 1-119 are pending.

Applicants' traversal, the amendment to the abstract, the amendment to claims 36, 52, 53, 58, 60-67, 74-75, 79-80, 83-84, 89-90, 97-107, and 110, and the addition of claims 117-119 in paper no. 11 is acknowledged and considered.

This application contains claims 86-87, 108-109, and 111-116 drawn to non-elected inventions and claims 10-14, 16-24, 26-35, 38-40, 42, 44, 71, and 92-93, 95-96 drawn to non-elected species with traverse in Paper No. 8. A complete reply to the final rejection must include cancellation of non-elected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Australia on 9/10/99. It is noted, that applicant have filed a certified copy of the Australian application as required by 35 U.S.C. 119(b).

Specification

The objection to the abstract is moot in view of the amendment to the abstract.

However, the disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (e.g. page 10, line 30, page 32, line 10, page 56, line 28,

page 62, line 28). Applicants are required to delete any embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Objections

The objection to claims 58, 61, 65-67, 74-75, 83, 98, 105, 107, and 110 is moot in view of the amendment to the claims.

Claim 67 is objected to because it encompasses a non-elected invention. See paper no. 8.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-9, 15, 25, 36-37, 41, 43, 45-70, 72-85, 88-91, 94, 97-107, and 110 remain and claims 117-119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-9, 15, 25, 36-37, 41, 43, 45-70, 72-85, 88-91, 94, 97-107, 110 and 117-119 as best understood, are readable on a genus of a recombinant microorganism that displays on its surface a binding moiety that competes with a ligand for binding to a receptor for the ligand, wherein the binding moiety comprises an oligosaccharide which comprises a sugar residue that is attached to an acceptor moiety by a glycosyltransferase that is encoded by an exogenous nucleic

acid which is present in the microorganism, wherein the genus of the recombinant microorganism is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 60-63, 67, 78-80, 78, 88, 99, 100-102 as best understood, are readable on a genus of a recombinant microorganism, wherein the microorganism has reduced production of external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic and/or is selected to provide some resistance to anti-microbial activity of micro-flora potentially resident in the gut and/or is resistant to the major families of colicins, wherein the genus of the recombinant microorganism is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 65, as best understood, are readable on a genus of a recombinant microorganism, wherein genes encoding at least one glycosyltransferase is modified to stabilize phase variation, wherein the genus of the recombinant microorganism is not claimed in a specific biochemical or molecular structure that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification contemplates production of a genus of recombinant microorganism that displays on its surface a binding moiety that competes with a ligand for binding to a receptor for the ligand, wherein the binding moiety comprises an oligosaccharide which comprises a sugar residue that is attached to an acceptor moiety by a glycosyltransferase that is encoded by an exogenous nucleic acid which is present in the microorganism. Furthermore, the as-filed specification contemplates that the acceptor moiety is endogenous to the microorganism and the glycosyltransferase is encoded by an exogenous nucleic acid. The disclosure further teaches that the acceptor moiety can consist of lipids or oligosaccharides on the outer surface of the microorganism (page 59). However, the as-filed specification and the art of record only provide sufficient description for sub-species (E.Coli) of a recombinant microorganism. The specification contemplates the production of Gm1, which is a mimicked by the LPS outer core of several Camplyobacter jejuni strains and using the sequence data the appropriate genes can be identified for assembly of the Gm1 mimic. One skilled in the art would consider the technology novel for describing a genus of the claimed recombinant microorganism. In addition, the genus of acceptor moiety of different microorganisms varies depending on the microorganism. For example, E.coli and mycobacterium are physically and structurally different from each other and each bacterium comprises of numerous genes including genes that are involved in transferring receptors to the outside surface of the microorganism and the specification does not disclose a representative species of acceptor moieties. The as-filed specification fails to provide sufficient

description of a genus of binding moieties that is considered an essential feature of the microorganism. This essential feature is required for one skilled in the art to practice the claimed invention because the binding moiety is used to compete with a ligand (e.g. receptor for a toxin) that binds to an endogenous receptor in an animal to reduce the level of that particular toxin in the animal. The state of the art discloses linking a Shiga toxigenic receptor (Stx2) to a mutated LPS in an E.coli to produce a recombinant E.coli (Paton et al. Nature Medicine, Vol. 6, pp. 265-270, 2000). Furthermore, Paton teaches that, "many bacterial and viral pathogens exploit oligosaccharide moieties of glycoproteins or glycolipids on the surface of eukaryotic cells as receptors for toxins, adhesions, or other ligands".

In addition, the specification contemplates a recombinant microorganism, wherein the microorganism has reduced production of external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic and/or is selected to provide some resistance to anti-microbial activity of micro-flora potentially resident in the gut and/or is resistant to the major families of colicins and/or the binding moiety comprises an oligosaccharide which comprises a sugar residue that is attached to an acceptor moiety by a glycosyltransferase that is encoded by an exogenous nucleic acid which is present in the microorganism wherein the acceptor molecule is an incomplete endogenous molecule and at least one of the exogenous glycosyltransferase competes with an endogenous glycosyltransferase to transfer said sugar molecule. The disclosure further contemplates a genus of a recombinant microorganism wherein one or more glycosyl transferase are naturally occurring and/or wherein genes encoding one or more glycosyl transferase are modified to stabilize phase variation. The as-filed specification provides sufficient description of glycosyl structures of receptors for toxins of bacteria (pages

27-28) and states that, "many glycosyltransferase are known, as are their polynucleotide sequences" (pages 10-18).

Furthermore, with respect to a genus of recombinant microorganisms wherein the microorganism has reduced production of external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic, the specification and the art of record only provide sufficient description of a species of bacteria that have produce a slime layer, capsule, or exopolysaccharide. The as-filed specification does not disclose a representative number of recombinant bacteria that produce the claimed external masking polysaccharide. The state of the art does not disclose a genus of microorganisms that produce external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic. Thus, in view of the state of the art, the disclosure does not sufficiently describe a genus of microorganism has reduced production of external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic.

Furthermore, with respect to a genus of microorganisms that is resistant to the major families of colicins. The specification contemplates a genus of the claimed microorganism but does not disclose a representative number of colicins to sufficiently describe a genus the claimed microorganisms. In addition, Brackelsberg et al. (Vet. Res. Commun., Vol. 21, abstract, 1997, Medline [online], Bethesda, MD USA: United States National Library of Medicine [retrieved on 6/28/02], Medline accession number 9266660) teaches that eight salmonella tymphimurium and eight salmonella dublin were isolated from cattle and none of the isolates produced colicin.

Thus, in view of the state of the art, the disclosure does not sufficiently describe a genus of microorganisms that are resistant to the major families of colicins other than from E.coli.

In addition, other than asserting that genes encoding one or more glycosyltransferases can be modified to prevent phase variation, the as-filed specification does not disclose a representative number genes to practice the genus of genes encoding all or some of the one of the glycosyltransferase are modifies to prevent phase variation. The specification described three genes from N.gonorrhoeae that are highly susceptible to slipped strand mispairing during replication (page 42, lines 25-32). However, the genes from N.gonorrhoeae are not a representative for the genus of genes encoding one or more glycosyltransferases that can be modified to prevent phase variation. One skilled in the art understands that phase variation is the switching of chemical structure (e.g. terminal LPS structure on a cell's exterior surface) and that the genus of the claims read on an enormous number of chemical structures (LPS). For example, the state of the art teaches lipo-oligosaccharide (LOS) biosynthesis loci from 11 Campylobacter jejuni strains expressing a total of 8 different ganglioside mimics in their LOS outer cores (Gilbert et al., JBC, Vol. 277, abstract, 2002). Gilbert further teaches that, "many pathogenic bacteria have variable cell-surface glycoconjugates...This variation is caused by the diversity of monosaccharide components and the linkage between them...The variation of these glycan structures can sometimes be correlated with a specific gene complement, but it is probable that other genetic mechanisms are also employed to create variable cell-surface glycoconjugates (page 327). Thus, the disclosure does not disclose a genus of recombinant microorganisms comprising genes encoding one or more glycosyltransferases that can be modified to prevent phase variation.

It is apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of acceptor moieties and/or a genus of a recombinant microorganism, wherein the microorganism has reduced production of external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic and/or is selected to provide some resistance to anti-microbial activity of micro-flora potentially resident in the gut and/or is resistant to the major families of colicins and/or a genus of a recombinant microorganism wherein all or some of the one or more glycosyl transferase are naturally occurring and/or wherein genes encoding all or some of the one or more glycosyl transferase are modified to stabilize phase variation as claimed; what is required is the knowledge in the prior art and/or a description as to the availability of a representative number of species of biochemical or molecular structures of recombinant microorganisms that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of a recombinant microorganism, wherein the microorganism has reduced production of external masking polysaccharide molecules other than said acceptor molecule to enhance exposure of the receptor mimic and/or is selected to provide some resistance to anti-microbial activity of micro-flora potentially resident in the gut and/or is resistant to the major families of colicins and/or a genus of a recombinant microorganism wherein all or some of the one or more glycosyl transferase are naturally occurring and/or wherein genes encoding all or some of the one or more glycosyl transferase are modified to stabilize phase variation. The claimed invention as a whole

is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. The claiming of a genus of recombinant microorganisms that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). The skilled artisan cannot envision the detailed structure of any genus contemplated by the claims that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Applicant's arguments filed 11/7/02 have been fully considered but they are not persuasive.

Applicants traverse the written description rejection for the following reasons: 1) in requiring specific biochemical or molecular structures for each embodiment, the office action applied an improper standard for adequacy of written description. The claimed invention is not a

novel DNA sequence but a novel microorganism that functions as a therapeutic agent. Emphasis solely on structure, as if a novel DNA sequence were claimed, is misguided and results in application of an incorrect standard for determining compliance with written description. The function of the invention correlates with the structure of the claimed invention. 2) The office action improperly rejected original claims as lacking adequate written description. The examiner has not presented evidence or reasoning to the contrary to rebut the presumption that adequate written description of the claimed invention is present in the application (page 23, line 15-18, page 24, lines 5-10, page 42, line 25-32). 3) The office action improperly required reduction to practice all embodiments to demonstrate possession of the claimed invention. The applicants have described the invention with sufficient clarity and precision to allow one skill in the art to make and to use the claimed genus thus satisfying the written description requirement (pages 10-18 and 26-36). Using methods described in the specification, applicants have provided examples of how to practice the invention (see examples 1 and 2). See pages 12-15 of paper no. 11.

Applicants' traversal is acknowledged and is not found persuasive for the following reasons: With respect to issue 1), the office action cites *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997) as one of the reasons that the claimed embodiment is not supported by the specification. The examiner acknowledged that Lily is directed to description of a claimed cDNA. However, the principle of the case is directed to sufficient guidance of function and structure of a genus cDNA sequences. The specification contemplates using a genus of recombinant microorganisms with specific functions (e.g. genes encoding one or more glycosyltransferase are modified to stabilize phase variation and/or a genus of recombinant microorganism is selected to provide some resistance to anti-microbial activity of micro-flora

potentially resident in the gut and/or a genus of the claimed microorganism is resistant to the major families of colicins; an exogenous nucleic acid which is present in the microorganism wherein the acceptor molecule is an incomplete endogenous molecule and at least one of the exogenous glycosyltransferase competes with an endogenous glycosyltransferase to transfer said sugar molecule thereto) without providing a representative number of structures for each genus claimed, so that one skilled in the art would know how to obtain (e.g. from a cell depository bank, ATCC) or make the claimed recombinant microorganisms.

In addition, the as-filed specification contemplates a genus of recombinant microorganism and only provides sufficient guidance for recombinant E.coli (gram-negative bacteria), which has a lipopolysaccharide (LPS) surface, which is used to express the acceptor moiety. However, many types of bacteria (gram-positive, Mycoplasma) do not have LPS on their surface and the as-filed specification does not disclose or how to obtain a genus of recombinant bacteria that meet the structural and functional limitation of the claimed genus. Furthermore, for the reasons set forth above, the support for each claimed genus is not disclosed by the as-filed specification.

Furthermore, with respect to issue 2), the specification does not provide sufficient description to overcome the written description rejection in view of the novelty of the claimed invention, the variability of the different species in each genus claimed, and the art of record cited by the examiner. The pages (e.g. page 23, line 15-18, page 24, lines 5-10, page 42, lines 25-32) cited in the applicants' traversal assert the same matter that was already cited in the claims and do not sufficiently disclosed support for any claimed genus.

With respect to issue 3), the office action is not requiring the reduction to practice of all embodiments. The state of the art teaches that, "Construction of a given mimic requires the identification of the specific glycosyltransferase required for synthesis, and insertion of gene encoding these into a heterologous host producing appropriate surface-expressed acceptor molecule" (Paton, pages 267-268). In view of the novelty of the claimed invention, the variability of each claimed genus (e.g. a genus of acceptor moieties, a genus of a recombinant microorganism that displays on its surface a binding moiety that competes with a ligand for binding to a receptor for the ligand, wherein the binding moiety comprises an oligosaccharide which comprises a sugar residue that is attached to an acceptor moiety by a glycosyltransferase that is encoded by an exogenous nucleic acid which is present in the microorganism wherein the acceptor molecule is an incomplete endogenous molecule and at least one of the exogenous glycosyltransferase competes with an endogenous glycosyltransferase to transfer said sugar molecule thereto, etc.), the office action is requiring a sufficient description of the different claimed embodiments and not the reduction to practice of all embodiments to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. For the reasons set forth above, the as-filed specification does not disclose a representative number of species for each genus claimed.

Thus, the as-filed specification does not provide sufficient guidance or factual evidence to overcome the 112 written description.

Claims 1-9, 15, 25, 36-37, 41, 43, 45-70, 72-85, 88-91, 94, 97-107, and 110 remain and claims 117-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification,

while being enabling for a recombinant bacterium comprising an exogenous nucleic acid encoding a glycosyltransferase that produces a specific sugar moiety, which is a mimic of a sugar moiety from a specific bacteriological toxin, when expressed on the cell surface attached to a surface-expressed acceptor molecule of the recombinant bacterium, wherein the recombinant bacterium is Escherichia coli (E.coli), and does not reasonably provide enablement for a genus of a recombinant microorganism comprising an exogenous nucleic acid encoding a glycosyltransferase that produces a receptor for a toxin and expressing the receptor on the surface of the microorganism and a method of delivering the recombinant microorganism to a mucosal surface of a mammal to reduce adherence of the pathogen or toxin produced by the pathogen to the mucosal surface. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Specifically, since the claimed invention is not supported by a sufficient written description (for possession of recombinant microorganism comprising genes encoding one or more glycosyl transferase are modified to stabilize phase variation and/or acceptor moieties and/or a recombinant microorganism, wherein the microorganism has reduced production of external masking polysaccharide molecules and/or is selected to provide some resistance to anti-microbial activity of micro-flora potentially resident in the gut and/or is resistant to the major families of colicins), particularly in view of the reasons set forth above, one skilled in the art would not have known how to use and make the claimed invention so that it would operate as intended, e.g. used for producing a mimic of a receptor for a toxin on the cell surface of a

recombinant microorganism using an acceptor moiety to transport the receptor to the outer surface.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention is in the field of producing a recombinant microorganism comprising an exogenous nucleic acid encoding a glycosyltransferase that produces a receptor for a toxin and expressing the receptor on the surface of the microorganism. The field of the invention lies in genetically modifying a microorganism to express an exogenous nucleic acid encoding a glycosyltransferase that is operably linked to an acceptor moiety that is expressed on the outer surface of the microorganism.

A brief description of the examples (pages 41-66) provided by the as-filed specification follow: Example 1 is the construction of a harmless recombinant E.coli capable of incorporating the trisaccharide Galalpha[1-4]GalB[1-4]Glc into the outer core region of the its lipopolysaccharide, wherein the trisaccharide is capable of binding several types of Shiga toxin. Furthermore, the example encompasses testing the recombinant bacterium to protect mice from fatal infection with STEC. Example 2 examined the capacity of oral administration of killed recombinant E.coli to protect mice from otherwise fatal challenge of STEC. Example 3 is the construction of a recombinant E.coli expressing globotetraose on its surface and examined its capacity to bind and neutralize STX2e in vitro. Example 4 teaches that C.difficle exotoxin A binds to several human glycolipids, all of which contain Galbeta[1-4]GlcNAc moiety and genes encoding transferase capable of assembling this epitope are also found in Neisseria IgT locus. Example 4 further contemplates the production of this epitope on recombinant bacterium and

asserts that the capacity to bind and neutralize exotoxin A can be assessed using a standard protocol. The example further points out that in vitro studies indicate that even stronger binding occurs between exotoxin A and the trisaccharide Galalpha[1-3]Galbeta[1-4]GlcNAc-, even though it is not present in humans, see Karlsson, 1998, Mol. Microbiology. Therefore, a strain expressing this epitope can be constructed by incorporation a gene encoding a transferase capable of forming the necessary epitope and a database search for a source of such a transferase. Example 5 contemplates the production of Gm1, which is a mimicked by the LPS outer core of several Camplyobacter jejuni strains and using the sequence data the appropriate genes can be identified for assembly of the Gm1 mimic. Examples 6-8 contemplate extrapolating from the model systems discussed above to block bacterial adhesion. Example 9 is the production of detection method using the recombinant microorganism constructed or contemplated by the above examples.

In view of the breadth of the claims, the working examples, the guidance provided by the as-filed specification; and the art of record, the claimed invention provides sufficient guidance for one skilled in the art to make and/or use a recombinant bacterium, wherein the bacterium is an E.coli, comprising and exogenous nucleic acid encoding a glycosyltransferase operably linked to a gene encoding an endogenous lipopolysaccharide that is expressed on the surface of the microorganism, wherein the expression of the exogenous nucleic acid results in a mimic of a receptor for a toxin of a pathogenic microorganism. However, the claimed invention is not enabled for the full scope of the clamed invention because the as-filed specification fails to provide sufficient guidance for one skilled in the art to make and use a genus of recombinant microorganism that displays on its surface a binding moiety that, when administered to an

animal, competes with a ligand for binding to a receptor for the ligand, wherein the binding moiety comprises an oligosaccharide which comprises a sugar residue that is attached to an acceptor moiety by a glycosyltransferase that is encoded by an exogenous nucleic acid which is present in the microorganism for the following reasons:

First, with respect to the claimed invention comprising the making and/or using of a genus of recombinant microorganism, the disclosure only provides sufficient guidance for one skilled in the art to make and/or use the bacterium, E.coli; because the as-filed specification fails to provide sufficient guidance for one skilled in the art to make and/or use an essential feature of the microorganism that is attaching a binding moiety (e.g. sugar residue, that is a mimic of a receptor on a pathogenic microorganism) to an acceptor moiety (e.g. lipopolysaccharide (LPS) that is transported to the exterior cell surface of the microorganism). This essential feature is required for one skilled in the art to practice the claimed invention because the binding moiety is used to compete with a ligand (e.g. receptor for a toxin) that binds to an endogenous receptor in an animal to reduce the level of that particular toxin in the animal. The state of the art teaches linking a Shiga toxigenic receptor (Stx2) to a mutated LPS in an E.coli to produce a recombinant E.coli and using the recombinant microorganism to protect mice from challenge with an otherwise 100% fatal dose of Shige toxigenic E.coli (Paton et al. Nature Medicine, 2000). Furthermore, Paton teaches that, "many bacterial and viral pathogens exploit oligosaccharide moieties of glycoproteins or glycolipids on the surface of eukaryotic cells as receptors for toxins, adhesions, or other ligands. Construction of a given mimic requires the identification of the specific glycosyltransferase required for synthesis, and insertion of gene encoding these into a heterologous host producing appropriate surface-expressed acceptor molecule" (Paton, pages

267-268). E.coli is a species of the genus, Gram-negative bacteria, which have a LPS, which is an essential component of bacterial cell surface of this genus. In addition, there are also other types of bacteria: Gram-positive, which do not have a LPS as part of the bacterial cell surface, Mycoplasma, which is a group of bacteria that lack a cell wall. The art of record is absent about using the surface-expressed LPS from E.coli as an accepted model for reasonably extrapolating to a genus of surface-expressed acceptor molecule in a genus of microorganism comprising gram-positive bacteria or Mycoplasma or LPS-surface expressed acceptor molecule in other gram-negative bacteria or any other type of bacteria. Therefore, in view of the unpredictability of the identifying a representative number of microorganism with a surface-expressed acceptor molecule that can be used for attaching an binding moiety to and expressing the cell's surface, it would take one skilled in the art an undue amount of experimentation to reasonably correlate from using a recombinant E.coli to practice the full breadth of the claimed invention.

In addition, with respect to the claimed invention encompassing making and using any binding moiety that when administered to an animal competed with a ligand for binding to a receptor for the ligand, the as-filed specification only provides sufficient guidance and/or factual evidence for one skilled in the art to make and/or use a sugar moiety and/or sugar moiety in the presence of suitable sugars because the genus of binding moiety is not sufficiently described in the as-filed specification. For example, the art of record teaches that many bacterial pathogens exploit oligosaccharide moieties of glycoproteins or glycolipids on the surface of eukaryotic cells as receptors for toxins, adhesions, or other ligands. Thus, it is not apparent how one skilled in the art would be able to reasonably extrapolate from making and/or using sugar moieties to any binding moieties, including glycolipids and glycoproteins because of the complex nature of these

receptors and the requirement for the correct three dimensional structure of these moieties and the correct expression of these moieties on the surface of a recombinant bacterium in order to successfully compete with a ligand for binding to a receptor for that ligand. In addition, the as-filed specification lacks sufficient guidance for the source for producing these moieties (glycoproteins and glycolipids) in a recombinant bacterium. Therefore, in view of the art of record and the lack of guidance provided by the as-filed specification, the claimed invention is only enabled for making and/or using sugar moieties.

Furthermore, there are concerns provided by the state of the art for expressing an exogenous nucleic acid encoding a glycosyltransferase operably linked to an appropriate surface-expressed acceptor molecule in a representative number of microorganisms. At the time the invention was filed, the as-filed specification provides sufficient guidance for expressing an exogenous nucleic acid in E.coli and one skilled in the art would have been enabled to make and/or use species of bacteria to express an exogenous nucleic acid encoding a glycosyltransferase in a culture and isolating exogenous nucleic acid from the culture. However, at the time application was filed and in view of the breadth of the claimed invention (recombinant microorganism), the as-filed specification fails to provide sufficient guidance for one skilled in the art to make and/or use a representative number of species for one skilled in the art to practice the full scope of the claimed invention because the disclosure does not provide sufficient guidance for what microorganisms are/are not considered enabled for one skilled in the art to make and/or use, which would require an undue amount of experimentation for one skilled in the art to reasonably extrapolate from the working examples using E.coli in the as-filed specification to a genus of microorganisms. For example, the state of the art teaches that

replication of plasmid DNA in gram-negative bacteria is dependent on three stages; initiation, elongation, and termination. The first stage, initiation depends on plasmid-encoded properties such as the replication origin (oriC) and in most cases, the replication initiation protein (Rep protein). Most plasmid studies exhibit a narrow host range limited to E.coli and related bacteria (Kues et al., Replication of plasmids in gram-negative bacteria, Micriobiol Rev., Vol. 53, 1989, (abstract) Medline [online], Bethesda, MD USA: United States National Library of Medicine [retrieved on 6/26/02], Medline accession number 2687680). The art of record also teaches that several species of oriC have been isolated (Moriya et al., Plasmid, Vol. 41, pp. 17-29, 1999). Moriya teaches that:

> Studies in E.coli have taken the lead in research of initiation mechanism of the bacterial chromosome replication and have provided considerable insight into this key regulation mechanism which is thought to be basically common in eubacteria. However, the picture is far from clear. In Bacillus Subtilis, our studies suggest that the mechanism that determines the time of initiation of chromosome replication is different from E.coli (page 17). Further analysis of initiation of replication using new technology will help elucidate the key mechanisms controlling bacterial cell cycle (page 26).

In view of the art of record and the lack of guidance provided by the as-filed specification for the making and/or using the genus of microorganism (e.g. bacteria), the as-filed specification only provides sufficient guidance for one skilled in the art to make and/or use E.coli in the claimed invention because of the reasons set forth above. Thus, it is not apparent as to how one skilled in the art reasonably extrapolates, without undue experimentation, from the scope of bacteria

(E.coli) to the full scope of the claimed invention that would display a binding moiety that competes with a ligand for binding a receptor for the ligand.

In addition, with respect to claims encompassing making and/or using a microorganism that is endogenously resistant to the major families of colicins in claims 63, 80, and 102, the as-filed contemplates using a genus of microorganisms listed above and in view of the state of the art only provide sufficient guidance for one skilled in the art to make and/or use E.coli because the as-filed specification only asserts that one skilled in the art can make and/or use a genus of microorganism without providing guidance on how this could be accomplished. One skilled in the art would know that a colicin is considered to be an antibacterial substances that are produced by strains of intestinal bacteria (as of *E. coli*) having a specific plasmid and that often act to inhibit macromolecular synthesis in related strains. To support the unpredictability of what microorganism endogenously produce colicin, Brackelsberg teaches that eight salmonella tymphimurium and eight salmonella dublin were isolated from cattle and none of the isolates produced colicin. Thus, in view of the state of the art, the disclosure does not provide sufficient guidance and/or factual evidence for what microorganisms are resistant to the major families of colicins other than E.coli. In view of the lack of guidance provided by the as-filed specification, it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from a plasmid in E.coli that is resistant to colicin to making and/or using a genus of microorganisms (gram-positive bacteria, Mycoplasma, yeast fungi, etc.) that are endogenously resistant to colicins.

In addition, with respect to claims encompassing making and/or using a genus of genes encoding one or more glycosyltransferases are modified to prevent or stabilize phase variation in

claims 65 and 75. Other than asserting that genes encoding one or more glycosyltransferases can be modified to prevent phase variation, the as-filed specification is absent of any examples for one skilled in the art to reasonably extrapolate from the assertion to making and/or using a representative number genes to practice the genus of genes encoding at least one of the glycosyltransferase are modifies to prevent phase variation. One skilled in the art understands that phase variation is the switching of chemical structure (e.g. terminal LPS structure on a cell's exterior surface) and that the breadth of the claims read on an enormous number of chemical structures (LPS). For example, the state of the art teaches lipo-oligosaccharide (LOS) biosynthesis loci from 11 Campylobacter jejuni strains expressing a total of 8 different ganglioside mimics in their LOS outer cores (Gilbert et al). Gilbert further teaches that, "many pathogenic bacteria have variable cell-surface glycoconjugates...This variation is caused by the diversity of monosaccharide components and the linkage between them...The variation of these glycan structures can sometimes be correlated with a specific gene complement, but it is probable that other genetic mechanisms are also employed to create variable cell-surface glycoconjugates (page 327). Therefore, in view of the lack of guidance provided by the as-filed specification for what amino acids are considered essential to stabilize or prevent phase variation, it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the assertion to the full scope of the making and/or using genes encoding glcosyltransferases that can be modified to prevent or stabilize phase variation.

Furthermore, with respect a method of administering a recombinant bacterium to a mammal to reduce adherence of a pathogen or a toxin produced by the pathogen in the mucosal surface of the mammal, the as-filed specification fails to provide sufficient guidance for how

controlled experiments using mice reasonably correlate to reducing adherence of a pathogen or a toxin produced by the pathogen in the mucosal surface of the mammal because the state of the art teaches that commencement of therapy immediately after challenge was 100% protective, but in a mammal setting such early intervention will be possible only for contacts of patients with confirmed cases, who have not yet, or have only just, become infected with a pathogenic microorganism, STEC (Paton et al., Infection and Immunity, Vol. 69, pp. 1389-1393, 2001). Thus, it is not apparent to one skilled in the art how to use the recombinant bacterium in any method sought forth in the claimed invention because of the unpredictability of determining when a mammal has, does not yet have or have only just become infected with a microorganism and if at later time points in the infection the recombinant microorganism can reduce the amount of toxin in the mammal. Therefore, it would take an undue amount of experimentation for one skilled in the art to reasonably extrapolate from controlled experiments to any method of reducing adherence of a pathogen or a toxin produced by the pathogen in the mucosal surface of the mammal.

Furthermore, with respect to a mimic of a receptor for a toxin in claims 1, 7, 68, 69, 88, and 90, the as-filed specification and the art of record only provide sufficient guidance for a toxin produced by bacteria because it is not apparent what other microorganisms produce toxins other than bacteria. Also, one skilled in the art would reasonably determine in view of the breadth of the claim that a toxin could be a chemical toxin and the as-filed specification lacks any description or factual evidence for any type of chemical toxin (e.g. radioactive material, carcinogens, etc.). Therefore, the as-file specification is only enabled for making and/or using a mimic of a receptor for a bacteria toxin.

Thus, in view of the In re Wands' Factors, the disclosure is only enabled for a recombinant bacterium comprising an exogenous nucleic acid encoding a glycosyltransferase that produces a specific sugar moiety, which is a mimic of a sugar moiety from a specific bacteriological toxin, when expressed on the cell surface attached to a surface-expressed acceptor molecule of the recombinant bacterium, wherein the recombinant bacterium is Escherichia coli (E.coli) and is not enabled for the full scope of the claimed invention because in view of the undue quantity of experimentation necessary to determine the parameters listed above for the starting material, the lack of direction or sufficient guidance provided by the as-filed specification for the production of a representative number of recombinant microorganism to practice the claimed invention. Furthermore, the lack of working examples for the demonstration or the reasonable correlation to the production of a genus of recombinant microorganism, in particular when the expression of a binding moiety attached to an acceptor moiety can compete with a toxin, the unpredictable state of the art with respect to the expressing an oligosaccharide attached to a LPS that is expressed on the cell's exterior surface, and the breadth of the claims drawn to any recombinant microorganism, it would require an undue amount of experimentation for one skilled in the art to make and/or use the full scope of the claimed invention.

Applicant's arguments filed 11/7/02 have been fully considered but they are not persuasive.

Applicants traverse the 112 enablement rejection for the following reasons: The office action has not established why one of skill could not use the genus as a whole without undue experimentation. Applicants assert that the examiner has not met his burden to establish a

reasonable basis to question the enablement provided by for the claimed invention. In the present application, one of skill would know how to avoid inoperative embodiments and make therapeutically active recombinant bacteria, without undue experimentation. The applicants disagree that that LPS is the only surface expressed acceptor molecule that is enabled by the specification because the specification at page 10, lines 19-24 clearly identifies a large number of potential extracellular acceptor molecules. The examiner has provided no objective reason to believe that recombinant glycosyltransferase of the appropriate specificity will be unable to alter acceptor molecules other than LPS molecules. The examiner appears to believe that the entire glycolipids or glycoprotein is required for binding by the pathogenic organism and thus must be recapitulated in the binding moiety of the receptor mimic but applicants point out that only the oligosaccharide moiety of the glycolipids or glycoprotein is used a receptor. Those of skill in will be able to determine whether a functional expression system is available for a given microorganism and will be able to avoid making inoperative embodiments of the clamed invention. Examiner present no evidence that bacterial genes or other genes lacking transcriptional processing signals (eg., CDNAs) cannot be expressed in eukaryotic cells. Applicants have provided assays to determine if glycosyltransferase genes are expressed. Inoperative embodiments can thus be determined without undue experimentation. Assays for colicin resistant microorganism other than E.coli are within the expertise of those of skill in the art. Routine experimentation described in the application would uncover the defect in glycosyltransferase activity allowing the user to select an operative embodiment of the recombinant enzymes (glycosyltransferase subject to phase variation) for use in the invention. Applicants disagree with the examiner alleging that the specification fails to provide support for

administration of the recombinant bacteria of the invention after infection with a pathogenic organism (See Example 2). It is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation. Applicants disagree that the use of non-bacterial toxins is not enabled by the specification because many examples of non-bacterial toxins are given in the specification. See pages 15-21 of paper no. 11.

The applicants' traversal and is not found persuasive for the following reasons: First, for the reasons set forth above, the office action has established sufficient reasons for why one skilled in the art could not use the genus as a whole without undue amount of experimentation including that the as-filed specification fails to provide sufficient guidance for one skilled in the art to make and/or use an essential feature of the microorganism that is attaching a binding moiety (e.g. sugar residue, that is a mimic of a receptor on a pathogenic microorganism) to an acceptor moiety (e.g. lipopolysaccharide (LPS) that is transported to the exterior cell surface of the microorganism). This essential feature is required for one skilled in the art to practice the claimed invention because the binding moiety is used to compete with a ligand (e.g. receptor for a toxin) that binds to an endogenous receptor in an animal to reduce the level of that particular toxin in the animal. The claimed invention is novel and the production of the claimed genus of recombinant microorganisms is not supported by the specification or art of record. For example, the art of record teaches that despite increasing attention to *Bifidobacterium* bacterium in many fields, little is known about its genetic property of this bacterium (Yazawa et al., Breast Cancer Research and Treatment, Vol. 66, pp. 165-170, 2001). Furthermore, the state of the art for transforming bacterium from the genus *Bifidobacterium* is

highly unpredictable as exemplified by Argnani et al. (Microbiology, Vol. 142, pp. 109-114).

The specification only provides sufficient guidance for how to use recombinant E.coli.

Furthermore, the court in Enzo 188 F.3d at 1374, 52 USPQ2d at 1138 states:

It is well settled that patent applications are not required to disclose every species encompassed by their claims, even in an unpredictable art. However, there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed.
In re Vaeck, 947 F.2d 48, 496 & n.23. 30 USPQ2d 1438, 1445 &n23 (Fed. Cir. 1991)(citation omitted). Here, however, the teachings set forth in the specification provide no more than a "plan" or "invitation" for those of skill in the art to experiment...; they do not provide sufficient guidance or specificity as to how to execute that plan. See Fiers v. Revel. 984 F.2d.1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993); In re Wright, 999 F.2d...[1557], 1562, 27 USPQ2d...[1510], 1514. [footnote omitted].

On this record, it is apparent that the as-filed specification and the applicants' traversal (See page 17 of traversal, which states, "one of skill would know how to avoid inoperative embodiments and make therapeutically active recombinant bacteria") provide no more than a plan or invitation in view of the art of record exemplifying the unpredictability of using any bacteria in the claimed invention, for those skilled in the art to experiment with different microorganisms to make and use the genus of recombinant microorganism as intended by the as-filed specification at the time the invention was made.

See also Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)

> ("Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable the public to understand and carry out the invention.")

In view of the art of record and the lack of guidance provided by the specification; the specification does not provide reasonable detail for what protocols are required for making and

using different microorganisms other than the sub-species E.coli, and it would take one skilled in the art an undue amount of experimentation to reasonably extrapolate from the scope listed above to the full breadth of claimed invention.

With respect to the traversal that only the oligosaccharide moiety of the glycolipids or glycoproteins is used as a receptor, the breadth of the claims encompasses entire glycolipids or glycoproteins and oligosaccharide moiety and the assertion is not found persuasive. See claim 1 compared to claim 37 or claim 51. In addition, the art of record teaches that many bacterial and viral pathogens exploit oligosaccharide moieties of glycoproteins or glycolipids on the surface of eukaryotic cells as receptors for toxins, adhesions, or other ligands. Thus, it is not apparent how one skilled in the art would be able to reasonably extrapolate from making and/or using sugar moieties to any binding moieties, including glycolipids and glycoproteins because of the complex nature of these receptors and the requirement for the correct three dimensional structure of these moieties and the correct expression of these moieties on the surface of a recombinant bacterium in order to successfully compete with a ligand for binding to a receptor for that ligand. In addition, the as-filed specification lacks sufficient guidance for the source for producing these moieties (glycoproteins and glycolipids) in a recombinant bacterium (See Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997)). Furthermore, the assertion that those of skill in the art would be able to determine whether a functional expression system is available for a given microorganism and will be available to avoid making inoperative embodiments is not found persuasive because the specification does not provide sufficient guidance or factual evidence for how to make the binding moieties comprising glycolipids and glycoproteins nor has applicants provided evidence to support their assertion.

Furthermore, with respect to the assertion that assays for colicin resistant microorganisms are within the expertise of those of skill in the art the assertion is not found persuasive because there is no evidence of record that teaches one skilled in the art how to make and use a representative number of the claimed microorganisms. The as-filed specification does not provide a working model for this claimed embodiment for one skilled in the art to reasonably extrapolate from identifying colicins observed in E.coli to the full scope of the claimed embodiment. Furthermore to support the unpredictability of identifying microorganism that endogenously produces colicin, see Brackelsberg. Also see Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997).

Furthermore, with respect to the assertion that routine experimentation described in the application would uncover the defect in glycosyltransferase activity allowing the user to select an operative embodiment of the recombinant enzymes (glycosyltransferase subject to phase variation) for use in the invention the assertion is not found persuasive because there is no evidence of record that teaches one skilled in the art how to make and use a representative number of the claimed microorganisms. The specification teaches three genes from N.gonorrhoeae that are subject to phase variation. The specification does not provide a working model for this claimed embodiment for one skilled in the art to reasonably extrapolate from the three genes from N.gonorrhoeae to the full breadth of the claimed embodiment. The disclosure does not provide what genes are required or what genes need to knock out of a representative number of recombinant microorganisms for one skilled in the art to practice the claimed invention. Furthermore the art of record teaches supports the unpredictability of making and

using the claimed genus. See Gilbert. Also see Genetech Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 1366, 42, USPQ2d 1001, 1005 (Fed. Cir. 1997).

Furthermore, with respect to the assertion that it is not necessary to specify the dosage or method of use if it is known to one skilled in the art that such information could be obtained without undue experimentation, the assertion is not found persuasive because the claimed invention is novel and there is no evidence of record that teaches one skilled in the art how to use a representative number of the recombinant microorganisms in the claimed methods. The specification teaches controlled experiments that display when the mouse was administered the pathogenic organism. The controlled experiments do not reasonably extrapolate to any claimed method because the time point at which the animal or mammal was infected will not be known. In a mammal setting such early intervention will be possible only for contacts of patients with confirmed cases, who have not yet, or have only just, become infected with a pathogenic microorganism, STEC (Paton et al., Infection and Immunity, Vol. 69, pp. 1389-1393, 2001).

In addition, with respect to the traversal that the use of non-bacterial toxins is enabled because the specification cites many types of non-bacterial toxins, the traversal is not found persuasive because the specification does not provide sufficient guidance or factual evidence for a genus of a toxin which embraces a chemical toxin (e.g. radioactive material, carcinogens, etc.) that the as-filed specification lacks sufficient guidance or factual evidence for making and using the full breadth of the claimed embodiment.

The rejection under 112 second paragraph for claims 1, 36, 52-53, 60, 62-65, 73-75, 79-80, 84, 89-90, 97-107, and 110 is moot in view of the amendment to the claims. See pages 22-23.

The 102(a) rejection for claims 1-8, 25, 46, 51, 53, 55-59, 63, 66-69, 74, 76, 78-80, 82-85, 88-90, 97-99, 102, and 104-107 is moot in view of the submission of foreign application AU PQ2757. See pages 23-24.

The rejection under 103(a) for claims 1-9, 15, 25, 37, 41, 43, 46, 51-52, 55-59, 63, 66-70, 73-74, 76, 78, 80, 82-85, 88-91, 94, 98-99, 102, and 104-107 is moot in view of the submission of foreign application AU PQ2757. See pages 23-24.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635
1/27/03

Scott D. Priebe

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PRIMARY EXAMINER